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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/719,619	11/20/2003	Matti Sallberg	TRIPEP.23AUSC1C	3662

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER	
LI, BAO Q	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 09/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/719,619	SALLBERG ET AL.	
	Examiner	Art Unit	
	Bao Qun Li	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-47,51-55,57-70 and 72-89* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-47, 51-55, 57-70, 72-89* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *8/10&11, 2006*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

This is a response to the amendment filed on 05/22/06. Claim 47 has been amended. New claim 89 has been added. Claims 1-33, 48, 56, 71 were canceled. Claims 34-47, 51-55, 57-70, 72-89 are pending and considered before the examiner.

Please note any ground of rejection(s) that has not been repeated is removed. Text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Election/Restrictions

In response to the previous office action, applicants assert that the claims that are linking claims, therefore, all viral antigens rather than limited to the HCV should be examined. Applicants' argument has been respectfully considered. All viral antigens are considered.

Terminal Disclosure (TD)

Applicants timely filed the TD over other Application No. 10,817,591 has been approved and it effectively overcomes the previous double patenting rejection of claims 34-47, 51-54, 57-69, 72-80 over claims 36-40, 42-55 and 57-65 of copending application 10,817,591.

Informality

The specification is objected because it contains a hyperlink in page 6 of current application. 37 CFR 1.57(d) states that incorporation by reference by hyperlink or other form of browser executable code is not permitted. In the instant case, the embedded hyperlinks and/or other forms of browser-executable codes are impermissible and require deletion.

Claim Rejections - 35 USC § 103

The 103 rejection is removed in view of the interview of the Applicants' attorney Eric Furman and TC 1600 QAS Yvonne Eyler on August 23, 2006.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 34-47, 51-55, 57-70, 72-89 are still rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing an enhanced mean antibody titer against HCV NS3 and stimulating the CD4+T cell specific against said HCVNS3 antigen or producing an enhanced mean antibody titer against HBV surface antigen comprising administration of a composition comprising a hepatitis C NS3 polypeptide or the commercial HBV surface antigen Engerix plus ribavirin at an effective amount in mice for a period of time, does not reasonably provide enablement for inducing at any condition with any or all antigen at any or concentration plus ribavirin at any concentration. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

3. The test of scope of the enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art would render undue experimentation (See United States v. Theketronic Inc., 8USPQ2d 1217 (fed Cir. 1988). Whether undue experimentation is required is not based upon a single factor but rather a conclusion reached by weighting many factors. Theses factors were outlined in Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in re Wands, 8USPQ2d 1400 (Fed. Cir. 1988) set forth below: 1). The nature of invention: 2). Scope of the claim; 3). Level of skill to perform the invention; 4). State of art; 5). Unpredictability in the field, 6). Number of working examples in the specification; 7). Amount of guidance provided by the specification.

4. In the instant case, the claimed invention is drawn to a method for producing an enhanced mean titer of IgG and activated CD4+ T cell against a specific viral antigen by administration of a composition contains HCV polypeptide of NS3 or HBsAg plus a ribavirin as a mix at a proper effective amount for a certain period of time of treatment.

5. However, the scope of the claims are directed to produce an enhanced immune response against anti any antigen by administering any antigen in combination with ribavirin in any concentrations together.

6. Applicant appears to have found that one very narrow combination of animal, ribivirin dose, specific antigen, and time to measurement results in an enhanced antibody production and lymphocyte proliferation. Applicant has not shown that this very limited set of experimental circumstances is predictive of the overall enhancing effect of ribivirin on any viral antigen in any animal under any circumstances and time period. For example, the specification only teaches to administrate a composition comprising the full length of NS3 at the dosage of 10 to 100 μg in combination of ribavirin at 0.1 to 10 mg or using HBsAg antigen of Engerix at 0.02 or 0.2 μg in combination with 1 mg of ribavirin in mice for at least 10 days or 3 weeks for the HCV NS3 or 6 weeks for HBsAg to induce an enhanced mean titer of antibody against the specific antigen and stimulate the CD4+ T cell activation against said HCV NS3 or HBsAg.

7. However, the specification does not teach any other viral antigen peptide is able to induce same enhanced immune responses. The specification does not teach any concentration of an antigen or ribavirin is able to produce the same immune response. The specification does not provide sufficient evidence or adequate guidance to support the broadly scope of the claims.

8. It is well known in the art that different antigens have different biological and immunological characteristics because they have different structures. Therefore, they also induce different immune responses because the host also response to different antigens in different way. For example, the HCV viral antigens favor to induce a predominantly TH1 type immune response and ribavirin also promotes the Th1 type immune response but suppress the Th2 type immune response as evidenced by Hultgren et al. (J. Gene. Virol. 1998, Vol. 79, pp. 2381-2391) and Fang et al. (J. Hepatology Nov. 2000, Vol. 33, pp. 791-798) and Tam et al. US patent No.5,677,097A). EBV nuclear antigen 1 different from other nuclear antigen of EBV virus, induces predominantly Th2 type immune response as evidenced by Steigerwald-Mullen et al. (J. Virol. 2000, Vol. 74, No. 15, pp. 6748-6759). They teach that EBNA1 and EBNA3C. Substantial proliferative responses by $CD4^+$ lymphocytes were demonstrated to both antigens in multiple, randomly selected donors. Surprisingly, we observed a striking and consistent difference in

cytokine response to EBNA1 and EBNA3C. EBNA1-specific $CD4^+$ T lymphocytes from multiple unrelated donors preferentially produced type 2-like cytokines in response to antigenic stimulation, while the response to EBNA3C was a characteristic type 1 response (See abstract and Figs. 4-6).

9. Moreover, it is well known in the art that any drug has toxicity and its therapeutic benefit only works within an appropriate concentration rages rather than any concentration. For example, the Hulgren et al. teach that the treatment of mice with 100 μM of ribavirin, the activation of the PHA-induced murine spleen cell is completely inhibited (See Fig. 2). If ribavirin is used at the 16 μg plus the LPS, the IL-12 cytokine product is increase; however, the IL-12 produce is inhibited if a higher concentration of ribavirin is used (See Fang et al. Fig. 6 on page 796). Heagy et al. teach that ribavirin inhibit the human PBMC cell proliferation when it is used in the range from 0.5 to 100 μM (J. Clin. Invest. 1991, Vol. 87, pp. 1916-1924, see Figs. 1-6).

10. Because the scope of the claims is broadly directed to any or all antigen with ribavirin at any concentration in any circumstance, the level of skill in the art to perform the full scope of invention is high and unpredictable.

11. Given the above analysis of the factors, which the courts have determined, are critical in asserting whether a claimed invention is enabled, it must be considered that the skilled artisan would have to conduct undue and excessive experimentation.

Double Patenting

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

11. Claims 34, 46, 51 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1 of the copending Application No. 11,409,670. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

12. In the instant case, both sets of claims are directed to a method for producing an enhanced antibodies response specifically to a viral antigen comprising administration of an immunogenic composition comprising a viral antigen and ribavirin.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

14. A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

15. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR. 3.73(b).

16. Claims 34, 44-47, 52-55 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 11,411,493. Although the conflicting claims are not identical, they are not patentably distinct from each other because the scopes of the current claims can be broadly explained either as a nucleic acid molecule and an amino acid molecule. If the claims are interpreted as nucleic acid, the scopes of

conflict claims are overlapping with the claim 1 of the copending application, because the claim 1 of the copending application contains all limitations that required by the claims 44-46, 52-55. To this context, the rejected claims are an obvious version of claim 1 of the copending application, and they are not patentable distinct each from other.

17. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 44-46, 52-55 and 81-84 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10,409,670.

19. In the instant case, the current claims 44-46, 52-55 and 81-84 are directed to method using an immunogenic composition comprising a viral antigen, preferably a HCV antigen, and ribavirin to increase the titer of IgG antibodies. The conflict claim 1 of the copending application is directed to a method for inducing an immune response comprising administration of a composition comprising a viral antigen and ribavirin, which contain all limitations of claims 44-46, and 52-55, and 81-84, which are present as an obvious version of claims 44-46, 52-55 and 81-84. Therefore, they are not patentable distinct each from other.

20. To this context, the conflict claims are obvious versions each from other absence of unexpected result.

21. This is a provisional obviousness-type double patenting rejection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao Qun Li whose telephone number is 571-272-0904. The examiner can normally be reached on 6:30 am to 3:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on 571-272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Bao Qun Li